Polyunsaturated Fatty Acids

(Wielonienasycone kwasy tłuszczowe)

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Abstract – The authors have discussed the chemical struture, major biochemical characteristics and biological significance of polyunsaturated fatty acids. Their particular focus was on the role of ***ω-3*** and ***ω-6*** acids in physiological processes and pathology development in human organism.

Key words – ω-3 and ***ω-6*** polyunsaturated fatty acids, biochemical characteristics, physiological significance, deficiency consequences

Streszczenie – Autorzy przedstawili budowę chemiczna, ważniejsze cechy biochemiczne oraz znaczenie biologiczne wielonienasyconych kwasów tłuszczowych. Szczególnie skupili się na roli ***ω-3*** i ***ω-6*** kwasów w procesach fizjologicznych i w narastaniu patologii w organizmie człowieka.

Słowa kluczowe – ***ω-3*** i ***ω-6*** wielonienasycone kwasy tłuszczowe, cechy biochemiczne, rola fizjologiczna, konsekwencje niedoboru.

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Authors' contributions to the article:

A. The idea and the planning of the study
B. Gathering and listing data
C. The data analysis and interpretation
D. Writing the article
E. Critical review of the article
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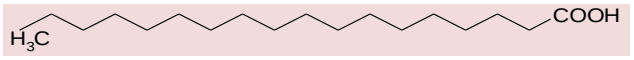
I. INTRODUCTION

In human organism, fatty acids predominantly have an esterified form and appear in natural fats and oils. Nevertheless, they are transported in the serum as non-esterified free fatty acids. Fatty acids in natural fats are usually a derivative of unbranched hydrocarbon chains with a hydrophobic methyl group at one end and a hydrophilic carboxyl group at the other (fig. 4). The methyl end of the molecule is referred to as **ω**-end, whereas the carboxyl group is at the **δ**-end. The names of acids are derived from the omega numbering system. In this system, carbon atoms are numbered starting at the methyl end. The properties of selected fatty acids are dependent on the length of the carbon chain as well as on the number and location of double bonds. Fatty acids can be divided into saturated (no double bonds), monounsaturated (one double bond) and polyunsaturated ones (≥ 2 bonds) [1-4].

Unsaturated fatty acids

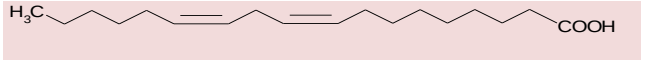


Stearic acid (C18:0)

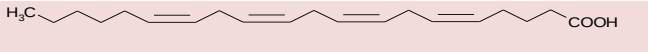
Monounsaturated fatty acids

Oleic acid (C18:1)

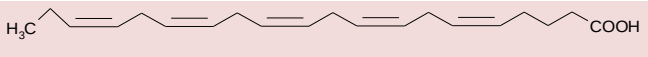
Polyunsaturated fatty acids



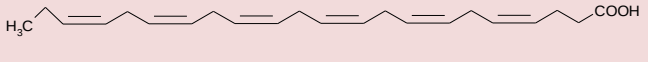
ω-6 Linoleic acid (C18:2, ω-6)*



ω-6 Arachidonic acid (C20:4, ω-6)



ω-3 Eikosapentaenoic acid (C20:5, ω-3)



ω-3 Docosahexaenoic acid (C20:5, ω-3)

Figure 4. Major fatty acids [4]

***Explanation**: * The first number is the amount of carbon atoms; the colon is followed by the number of double bonds. The data after the comma is the location of the first double bond, starting the count at the methyl end.*

Polyunsaturated fatty acids (***PUFAs***) can be divided into two subgroups: ***ω-3*** and ***ω-6***. In ***ω-3 PUFAs***, the first double bound is located after the third carbon atom (C-3) (table 3), whereas in ***ω-6 PUFAs*** it is after C-6. ***ω-3*** and ***ω-6*** acids are considered essential fatty acids as human organism cannot synthesise them and they need to be provided in food [3,4].

Table 3. ω-3 polyunsaturated fatty acids of physiological significance [5]

	Systematic name	*Common name*
C18:3, ω-3	6,12,15- octadecatrienoic acid	Alpha-linolenic acid
C20:5, ω-3	5,8,11,14,17- eicosapentaenoic acid	Timnodonic acid
C22:5, ω-3	7,10,13,16,19- docosapentaenoic acid	Clupanodonic acid
C22:6, ω-3	4,7,10,13,16,19- docosahexaenoic acid	Cervonic acid

***Explanation**: * The first number is the amount of carbon atoms; the colon is followed by the number of double bonds. The data after the comma is the location of the first double bond, starting the count at the methyl end.*

Alpha-linolenic acid is transformed during dehydrogenation and chain lengthening to fatty acids of 20 and 22 carbon atoms, which are referred to as *long chain essential fatty acids [Gerster (1998)]*. The one of most biological significance among them is eicosapentaenoic acid – a precursor to Series 3 prostaglandins (PG_3), thromboxane (TX_3) and leukotriene (fig. 5). PG_3 and TX_3 inhibit the arachidonate release from phospholipids as well as PG_2 and TX_2 formation. PG_3 has stronger antiaggregatory effect on platelets as compared to PGI_2, whereas TXA_3 is a weaker thrombocyte aggregation factor than TXA_2. As a result, the dominant biological effect of eicosanoids from ***ω-3 PUFAs*** is platelet aggregation and anti-inflammatory effects [3-9].

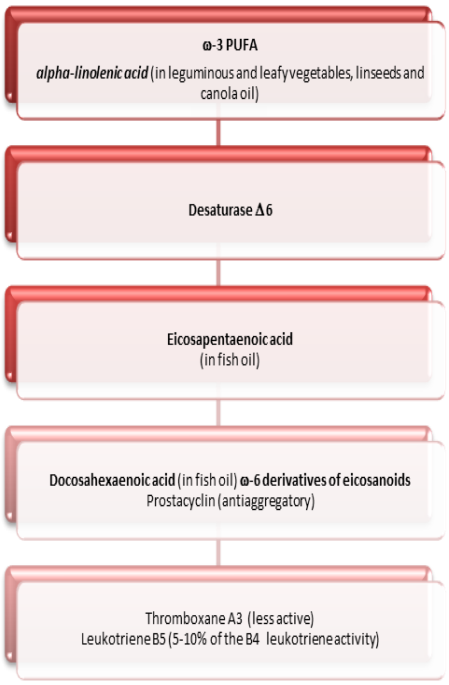


Figure 5. The course of desaturation and lengthening ω-3 polyunsaturated fatty acids and the formation of their eicosanoids [3]

II. THE ROLE OF ω-3 POLYUNSATURATED FATTY ACIDS IN PHYSIOLOGY AND PATHOLOGY

ω-3 PUFAs are, similarly to other kinds of fatty acids, not only an energy source but also a carrier of lipid soluble vitamins. What is more, they participate in the biosynthesis of prostanoids and transportation as well as oxidation of cholesterol. Additionally, they perform

structural functions as they are one of the components of membrane lipids [3,6,8,10,11,12].

One of the biologically relevant properties of ***ω-3 PUFAs*** is related to their anti-coagulant effects [3]. For instance: eicosapentaenoic acid inhibits the synthesis of thromboxane A_2 and prostaglandin that causes platelet aggregation and vasospasms [4,5,12-15]. The ω-3 acids also lower the concentration of fibrinogen and increase the concentration of tissue plasminogen activator [4]. What is more, the acids in this group lower the concentration of blood triglycerides [4,5,14-16]. They also affect the blood cholesterol level. However, the biological effects they have are interpreted in various ways. Some authors [2] report the increase in the HDL_2 concentration after the intake of ***ω-3 PUFAs***, whereas others [15,16] confirm the decrease in HDL_3 containing substantial amounts of triglycerides. There are also reports claiming that ***ω-3 PUFAs*** may increase the susceptibility of LDL cholesterol to oxidation. Some indicate that ***ω-3PUFAs*** have hypotensive effects [17]. Recently, there has been a lot of interest in potentially antiarrhythmic effects of these fatty acids. It is believed that ***ω-3 PUFAs*** stabilise the electrical activity of cardiac muscle cells by blocking the ion channels, prolonging the relative refractory period [10,18]. Also, their positive effects on endothelium are emphasised [18]. The studies of animal models showed that ***ω-3 PUFAs*** have antiaherogenic effects (table 4). These properties, however, are retained mainly by the acids of marine origin [3,19,20].

Table 4. The impact of **ω-3 PUFAs** on mediators of atherosclerosis [3-5,21]

Factor	Function	The impact of *ω-3 PUFAs*
Arachidonic acid	The precursor of eicosanoids, its effect is platelet aggregation	↓
Thromboxane A_2	Platelet aggregation, vasoconstriction	↓
Prostacyklin	Prevents from platelet aggregation, vasodilatation	↑
Tissue plasminogen activator	Intensifies fibrinolysis	↑
Fibrinogen	Coagulation factor	↓
Platelet activation factor	Activates platelets and leukocytes	↓
Platelet-derived growth factor	A chemoatractant and a mitogen of smooth muscles and macrophages	↓
Endothelium-derived relaxing factor	Decreases the vasospastic artery reaction	↑
Triglycerides and chylomicrons	Participating in postprandial lipidemia	↓
High-density lipoproteins	Decrease the risk of ischaemic heart disease	↑
Lipoprotein (a)	Atherogenic Lipoprotein	↓

Explanation: ↓ *- decrease* ↑ *- increase*

Certain works also emphasise a negative impact of ***PUFAs*** on human organism. That is predominantly connected with the promotional role of linoleic acid and its 20-carbon homologue - arachidonic acid in neoplastic processes (fig. 6) [3,5,22].

The interest in the role of 20-carbon unsaturated fatty acids in carcinogenesis resulted from the observation of increased prostaglandin concentration in neoplasms in humans. Presently, it is acknowledged that the inhibition or stimulation of carcinogenesis is dependent on the type of prostaglandin, its concentration and the type of the target cell (neoplasm type) [3-5]. For instance, PGE_2 and PGD_2 have inhibitory effects, whereas TXA_2 and malonylodialdehyde are stimulating factors for cancer growth [3].

Presently, the participation of ***PUFAs*** in carcinogenesis in human organism is associated predominantly with a regulatory (agonistic or antagonistic) influence of the acids on the receptors with their own tyrosine kinase. The effect of ***ω-3 PUFAs*** most probably consists in blocking the receptors, hence the increase in the concentration of the acids may contribute to cancer growth prevention [3-5,15].

The receptors of this group include *epidermal growth factor, EGF* and *proto-oncogenes C-erbB2 (neu)* and *c-erbB3* [2-5].

The transmission of the signal from the receptor to tyrosine kinase is a multistage process. After cytokine (or an antagonist) is bonded, the receptor dimerises and undergoes autophosphorylation. After that, the kinase which is an integral part of the receptor phosphorylates proteins with homological sections with *c-Src (SH2)*, which constitute a beginning to several signal transduction pathways to the nucleus (fig. 8).

The family of cytoplasmic *c-Src tyrosine kinases* is constituted by at least nine proteins of similar structure. The proteins stimulate the *c-Ras* signal pathway on one side and *phosphatidylinositide 3-kinase* one the other. *Ras* protein counters the *MAP (mitogen activated protein) kinases* and *serine/threonine kinases* cascade. These kinases, coded by the *c-raf* gene, participate in the transmission of mitogen signal from membrane receptor to nucleus. Presently, it is acknowledged that *Ras* protein plays a major part in neoplastic transformation also by means of activating other oncogenes, including: *Pim-1, Mos, Raf, Myc, Myh, Fos, Jun, ErbA, Ets* [15,23,24].

What is more, the risk of cancer is increased by the fact that ***PUFAs*** are likely to undergo oxidation processes as a result of which hydroxides, endogenic peroxides, epoxy compounds and free radicals are formed. These compounds may damage the cell membrane structure, trigger-

ing the release of ions stored in cell organelles (fig. 9). The ions catalyse the formation of new radicals, which continue to destroy the lipid structure. The radicals released may also damage the DNA structure and lead to the formation of mutagenic and carcinogenic products [5].

Additionally, ***PUFAs*** increase the fluidity and permeability of cell membranes, facilitating carcinogenic compounds to penetrate the cells [2,3].

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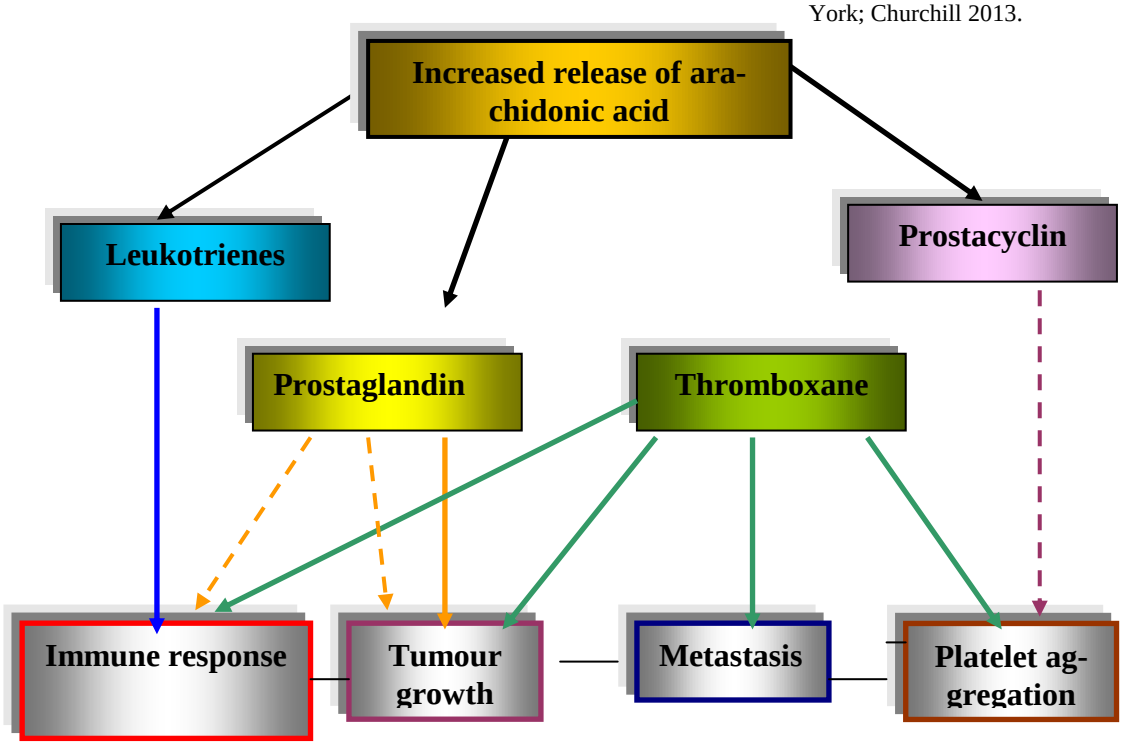

Figure 6. The impact of arachidonic acid metabolites on cancer growth [3-5]
Explanation*: continuous line - stimulation, dashed line - inhibition*

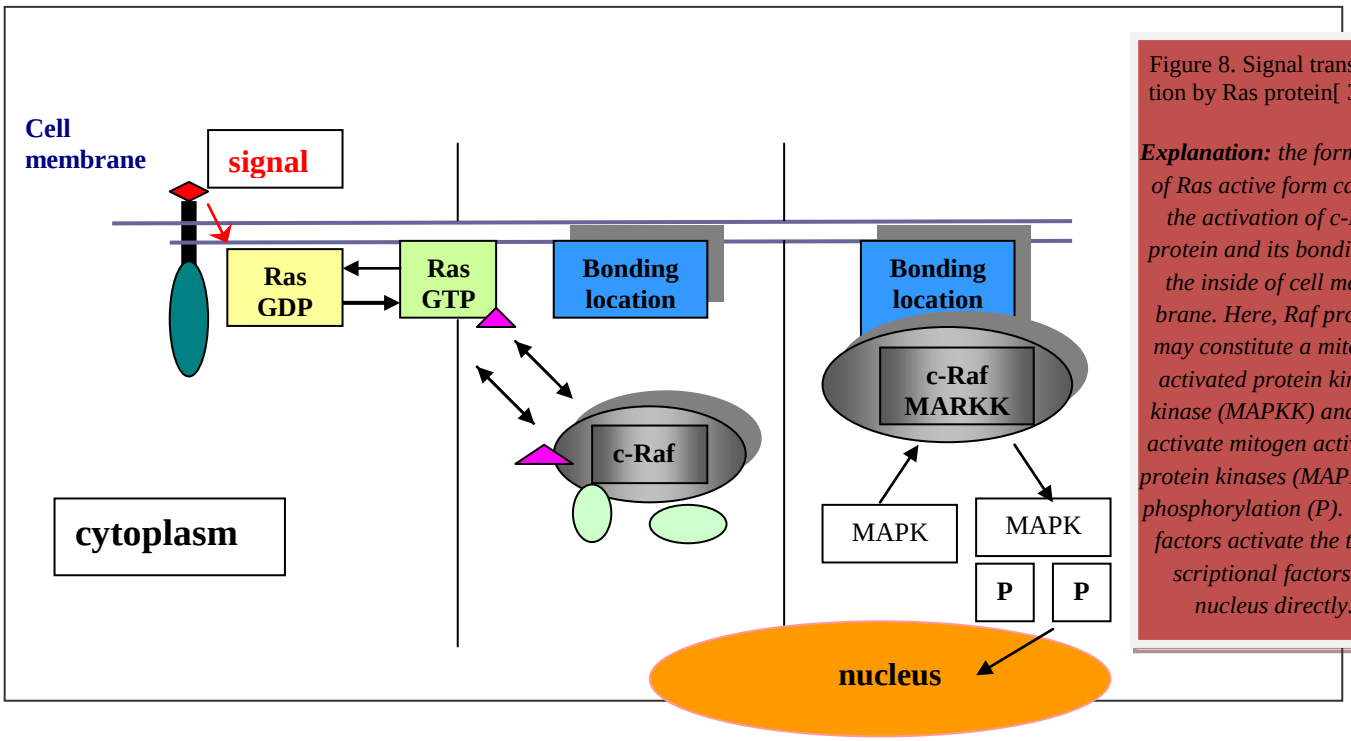

Figure 8. Signal transduction by Ras protein[3-5].

Explanation: *the formation of Ras active form causes the activation of c-Raf protein and its bonding to the inside of cell membrane. Here, Raf protein may constitute a mitogen activated protein kinase kinase (MAPKK) and can activate mitogen activated protein kinases (MAPK) via phosphorylation (P). These factors activate the transcriptional factors in nucleus directly.*

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